SYPHILIS REINFECTIONS AMONG HIV+ AND HIV- PATIENTS: A RETROSPECTIVE STUDY

883

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BACKGROUND

Syphilis infection does not lead to definitive immunity against reinfection and crucial aspects of repeated episodes of syphilis are far from being cleared.
Our Infectious Disease Unit assists 3841 HIV+ patients, with a dedicated clinic for sexually transmitted diseases which is part of the Italian Sentinel Surveillance System (SSS).
We aimed to compare demographical, serological and clinical features of syphilis reinfections in HIV+ and HIV- patients.

METHODS

We retrospectively evaluated syphilis notifications from January 2013 to December 2021. We have split our sample between HIV+ and HIV- groups.

Table 1 Demographical features of our sample

	HIV-	HIV+	Total	p-value
Population (n, %)	316 (48%)	**347 (52%)**	653	
Sex				**<.001**
Males (n, %)	176 (56%)	**332 (96%)**	508	
Females (n, %)	140 (44%)	15 (4%)	155	
Age				0.5
Median (Minimum, Maximum)	36 (12-83)	**40 (12-75)**		
Origin				**<.001**
Europe (n, %)	230 (73%)	**292 (84%)**	522	
Other (n, %)	86 (27%)	55 (16%)	141	
Sexual Orientation				**<.001**
Homosexual/Bisexual (n, %)	39 (17%)	**260 (78%)**	299	
Heterosexual (n, %)	184 (83%)	73 (22%)	257	
Syphilis Stage during First Infection				**<.001**
Late Latent (n, %)	**228 (78%)**	**158 (51%)**	386	
Other (n, %)	63 (22%)	150 (49%)	213	
Reasons for Syphilis Test performance				**<.001**
Screening/Follow Up (n, %)	81 (47%)	**257 (80%)**	338	
Symptom's onset (n, %)	**91 (53%)**	64 (20%)	155	
Syphilis episodes before study period				**<.001**
Before 2013 (n, %)	45 (14%)	143 (41%)	188	
After 2013 (n, %)	269 (86%)	205 (59%)	474	
Presence of Syphilis Reinfections				**<.001**
Yes (n, %)	61 (19%)	**209 (60%)**	270	
No (n, %)	255 (81%)	138 (40%)	393	
Number of syphilis episodes				**<.001**
Median (Minimum, Maximum)	1 (1-3)	**1 (1-7)**		

Considering *serological response* during *syphilis reinfection*, our analysis shows that *no statistical* difference was observed between *HIV+* and *HIV-*.
Serological response in *syphilis reinfections* in HIV+ is merely less likely to be rapid.

Demographical, clinical characteristics and risky habits were considered. All patients were effectively treated. Number of syphilis reinfections was recorded and serological response was assessed at 6 month and 12 months after treatment. A patient was considered as a serological responder in case of seroreversion or 4-fold decline in non treponemal titers.
Pearson's Chi-squared test with simulated p-value (based on 2000 replicates) and Welch Two Sample t-test were used to assess demographical (**Table 1**) and serological response (**Table 2**) in the two groups. Multivariate analysis was performed to assess factors associated with serological response of syphilis reinfections in HIV+ patients (**Table 3**).

RESULTS

Syphilis was diagnosed in 653 patients of whom 347 (52%) were HIV+. Among HIV+, patients were mostly male (96%), European (84%), homosexual or bisexual (78%) and with a median age of 40 years old (range 12-75). During the study period, syphilis first infection was diagnosed mostly in late-latent stage both among HIV- (78%) and HIV+ (51%) groups.

Table 2 Serological response

	HIV-	HIV+	p-value
Reinfection Episodes (n, %)	54 (14%)	**328 (86%)**	
Seroreversion			
6 months (n, %)	7 (21%)	62 (23%)	0.8
12 months (n, %)	6 (21%)	70 (32%)	0.3
Serological-Non-Response			
6 months (n, %)	20 (61%)	130 (48%)	0.2
12 months (n, %)	14 (50%)	75 (34%)	0.1
Serofast Status			
6 months (n, %)	8 (24%)	86 (39%)	0.2
12 months (n, %)	10 (36%)	94 (35%)	0.8

Syphilis tests were performed as annual screening in HIV+ patients (80%), whereas in HIV-, a treponemal or non-treponemal-test was carried out mostly for symptoms appearance (53%). Among HIV+, up to 6 episodes of syphilis reinfection were recorded in the same patient. Syphilis reinfections were predominantly diagnosed in HIV+ patients (86%). No significant statistical difference was seen in serological response between HIV+ and HIV- reinfection. Among HIV+, seroreversion rate raised with the increasing of time (23% at 6 months, 32% at 12 months), while SNR decreased at 6 and 12 months after treatment (48% at 6 months, 34% at 12 months).

Table 3 Multivariate analysis on serological-non-responders

Characteristic	exp(Beta)	95% CI	p-value
Sex			
Male	2.67	0.25, 28.4	0.4
Age			
>50	0.58	0.20, 1.67	0.3
CD4 at Diagnosis			
<=350	1.03	0.35, 3.00	>0.9
HIV-RNA			
Positive	0.89	0.48, 1.63	0.7
RPR			
> 1:16	**2.26**	1.14, 4.51	**0.020**
Time			
12 months	**0.38**	0.22, 0.65	**<0.001**
CI = Confidence Interval			

In HIV+ patients, homosexual/bisexual orientation resulted the only factor associated with syphilis reinfection (OR 1.54). High (>1:16) RPR titer (OR 2.26, 95%CI 1.14-4.51, p=0.02) and evaluation at 12 rather than 6 months after treatment (OR 0.38, 95%CI 0.22-0.65, p<0.001) were associated to a lacking serological response.

CONCLUSIONS

Syphilis reinfections are predominantly diagnosed in HIV+ men who have sex with men. Although especially in HIV patients each additional episode of syphilis may result in an altered immune response, seroreversion rate are not statistically different among HIV+ and HIV-. In HIV+ patients, the only baseline factor associated to an increased risk of non-response was RPR titer >1:16, while the assessment at 12 months after treatment increases the possibility to detect serological response.